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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,532	07/19/2002	Daniel R. Soppet	PF168P3	5548

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,532	SOPPET ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,26-31 and 38-42* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-31 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *11,26-31 and 38-42* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Appendix A

DETAILED ACTION

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Bridget Bunner.

Status of Application, Amendments and/or Claims

The amendments of 11 October 2005, 03 May 2005, and 28 February 2005 have been entered in full. Claim 11 is amended and claims 1-10, 12-25, 32-37, and 43-47 are cancelled.

Election/Restrictions

Applicant's election with traverse of Group IV-K, claims 11 and 26-47, drawn to polypeptides comprising amino acid residues 1(2)-425 of SEQ ID NO: 2 in the reply filed on 11 October 2005 is acknowledged. The traversal is on the ground(s) that the members of the Markush group in amended claim 11 are so closely related (because each is a part of SEQ ID NO: 2) that a search and examination of the entire claim can be made without serious burden. This is not found persuasive because each group (IV-A through IV-K) represents a patentably distinct product with distinct physical and functional characteristics. As discussed in the previous Office Action of 09 August 2005, the search for more than one product would be burdensome on the examiner and the USPTO's resources because each search for a portion of a disclosed amino acid sequence requires a *separate, non-coextensive* "word search" of the amino acid databases. Thus, due to the use of "comprising" language recited in claim 11, the search for a polypeptide comprising amino acids 1 to 425 of SEQ ID NO: 2 would not necessarily reveal art pertaining to, for instance, a polypeptide sequence *comprising* amino acids 73 to 82 of SEQ ID NO: 2, as the latter could be found embedded in a completely different protein.

The requirement is still deemed proper and is therefore made FINAL.

If Applicant wishes to pursue the matter further, a petition should be filed in accordance with 37 CFR 1.144.

It is noted that at pg 4 of the Response, Applicant requests clarification of the meaning of the phrase "correspond to the elected invention". In the Office Action of 09 August 2005, the Examiner simply was requesting that Applicant list the claims that recite the elected invention of Group IV-K (amino acids 1(2)-425 of SEQ ID NO: 2). Thus, the claims that recite the polypeptide comprising amino acids 1(2)-425 of SEQ ID NO: 2 are claims 26-31 and 38-42.

Claim 11 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11 October 2005.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 26-31 and 38-42 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 2-3 of the Office Action of 01 November 2004 are *withdrawn* in view of the amended specification and submission of a legible copy of pg 38 of the specification (28 February 2005).

2. The rejection of claims 43-47 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pg 13-15 of the Office Action of 01 November 2004 is *withdrawn* in view of the cancellation of claims 43-47 (11 October 2005).

3. The rejection of claims 11 and 32-37 under 35 U.S.C. § 112, first paragraph (deposit rules) as set forth at pg 15-17 of the Office Action of 01 November 2004 is *withdrawn* in view of

amended claim 11, cancelled claims 32-37 and the submission of a statement by the attorney of record (28 February 2005 and 11 October 2005).

4. The rejection of claim 11 under 35 U.S.C. § 102(b) and 35 U.S.C. § 102(e) as set forth at pg 17 of the Office Action of 01 November 2004 is *withdrawn* because the claim is drawn to a nonelected invention.

5. The rejection of claims 11 and 26-30 under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(e) as set forth at pg 17-18 of the Office Action of 01 November 2004 is *withdrawn* because claim 11 is drawn to a nonelected invention and Bergsma et al. do not teach a polypeptide comprising amino acid residues 1 to 425 of SEQ ID NO: 2 of the instant application.

6. The rejection of claims 11 and 26-31 under 35 U.S.C. § 102(e) as set forth at pg 18 of the Office Action of 01 November 2004 is *withdrawn* because claim 11 is drawn to a nonelected invention and Hagan et al. do not teach a polypeptide comprising amino acid residues 1 to 425 of SEQ ID NO: 2 of the instant application.

Specification

7. The disclosure is objected to because of the following informalities:

7a. Page 9, lines 31-32 teach a protein of 402 amino acid residues. However, the none of the amino acid sequences disclosed in the application (such as SEQ ID NOs: 2, 4, 6) have 402 amino acids.

Appropriate correction is required.

Claim Rejections - 35 USC §101 and § 112, first paragraph

8. Claims 26-31 and 38-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established

utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for claims 11 and 26-47 at pg 3-9 of the Office Action of 01 November 2004.

Specifically, claims 26-31 are directed to an isolated protein comprising amino acid residues 1 to 425 of SEQ ID NO: 2. Claims 38-42 are directed to an isolated protein comprising a polypeptide which is at least 95% identical to amino acid residues 1 to 425 of SEQ ID NO: 2. The claims also recite that the amino acid sequence further comprises a heterologous polypeptide. The claims recite a composition comprising the isolated protein and a carrier. The claims recite that the isolated protein is glycosylated.

Applicant's arguments (28 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the specification of the instant application discloses that the molecule of the claimed invention is a novel member of the G-protein coupled receptor family isolated from a cDNA library prepared from human hypothalamus tissue (pg 9, lines 29-32). Applicant argues that the specification teaches the hypothalamus is believed to play a central role in the regulation of feeding behavior and in the control of energy balance in mammals (pg 2, lines 16-25). Applicant also states that the specification teaches the claimed invention is useful in the prevention and/or treatment of a number of diseases and disorders, including obesity and hyperlipidemia. At page 8 of the response of 28 February 2005, Applicant contends that the Sakurai et al. reference (Cell 92(4): 573-585) corroborates (as disclosed by the Applicant) that the claimed invention may be useful in the prevention and/or treatment of diseases and disorders, including obesity and hyperlipidemia. Applicant states that Sakurai et al. demonstrates that

"OX1R" (which is 99.8% identical to SEQ ID NO:2 of the instant application) is a neuropeptide receptor member of the G-protein coupled receptor family that regulates feeding behavior in rats (pg 582 of Sakurai et al.).

Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application teaches that the polynucleotide encoding the claimed polypeptide was discovered in a cDNA library derived from human hypothalamus (pg 9, lines 29-30). The specification teaches that it is structurally related to the G protein-coupled receptor family and that the receptor protein "exhibits the highest degree of homology to human neuropeptide Y receptor protein" (pg 9, lines 31-32; pg 10, line 1). Furthermore, the specification discloses that resulting variant constructs preferably "have an increased neuropeptide receptor activity or function, while the remaining neuropeptide receptor activities or functions are maintained. More preferably, the resulting constructs have more than one increased neuropeptide receptor activity or function, while the remaining neuropeptide receptor activities or functions are maintained" (pg 31, lines 30-33; pg 32, lines 1-3). However, the specification of the instant application does not teach any specific activities or functions of the claimed receptor polypeptide of SEQ ID NO: 2. The specification does not teach any specific disorders (particularly obesity and hyperlipidemia) or conditions that are associated with altered levels or forms of the claimed neuropeptide receptor polypeptide. The specification at pages 161-213 and 229-231 only lists hundreds of diseases and disorders that the claimed polypeptide of SEQ ID NO: 2 could possibly be used to diagnose and prevent/treat. In order for a polypeptide to be useful, as asserted, for diagnosis or prevention/treatment of a disease, there must be a well-established or disclosed correlation or relationship between the polypeptide and a

disease or disorder. Such is not the situation in the instant application. Significant further experimentation would be required of the skilled artisan to identify individuals with a disease correlated to altered levels or forms of the claimed neuropeptide receptor polypeptide and to determine the route of administration of the protein, as well as quantity and duration of treatment. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Additionally, although the "OX1R" receptor polypeptide of Sakurai et al. is 99.8% identical to the polypeptide of SEQ ID NO: 2 of the instant application, Sakurai et al. discovered that "OX1R" binds novel peptide ligands, orexin-A and orexin-B (pg 577, col 1). Sakurai et al. point out that "OX1R" (also known as HFGAN72 receptor) is structurally similar to other neuropeptide receptors, but hypothesized that OX1R is the receptor for orexins, another class of small regulatory peptides (pg 577, col 1, first full paragraph). Sakurai et al. even state that competitive radioligand binding assays performed with OX1R and orexin-A were not inhibited by any of the several unrelated peptides tested, *including neuropeptide Y* and endothelin-1 (pg 577, col 1, first full paragraph). The current state of the art also indicates there are many different hypothalamic neurotransmitters involved in the control of feeding, including neuropeptide Y, melanocortins, and orexins (and their respective receptors) (see for example, Williams et al., Phys Behav 74: 683-701, 2001; Williams et al., Proc Nutr Soc 59: 385-396, 2000). However, the specification of the instant application discloses that the claimed polypeptide of SEQ ID NO: 2 is a receptor "for ligands, both known and unknown, which modulate the activity of cells in both central nervous system and peripheral tissues regulated by the central nervous system. Examples of such ligands are neuropeptide Y, substance P, the

human *ob* gene product and neurokinin B" (pg 9, lines 5-8). The specification also discloses that an embodiment of the invention includes processes of administering compounds to a host which bind to and inhibit activation of the receptor, "which are useful in the prevention and/or treatment of Alzheimer's disease, Type II Diabetes Mellitus, epilepsy, stress, anxiety, hypertension, cardiovascular disease, psychotic conditions and obesity caused by neuropeptide Y" (pg 5, lines 18-23). Thus, the Examiner has broadly interpreted the specification as teaching that the claimed receptor of SEQ ID NO: 2 may possibly bind many ligands, such as neuropeptide Y. However, as indicated above, Sakurai et al. teach that neuropeptide Y does not bind the OX1R receptor (the polypeptide of SEQ ID NO: 2 of the instant application). Additionally, unlike Sakurai et al. (pg 580, 1st full paragraph), the instant specification does not specifically disclose that the claimed receptor polypeptide of SEQ ID NO: 2 is involved in the stimulation of food intake.

The polypeptide of the instant application (SEQ ID NO: 2) is not supported by either a credible, specific and substantial ("real-world") asserted utility or a well-established utility. The polypeptide does not have a substantial utility because basic research is required to study the properties and activity of the claimed polypeptide of SEQ ID NO: 2. The specification of the instant application does not disclose the function of the polypeptide and only recites prophetic examples of how the claimed polynucleotide and polypeptide can be utilized in various assays (pg 141-145, 158-224, 229-239, for example). It is clear from the instant specification that the polypeptide described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and

substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an Appellant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Until some actual and specific significance can be attributed to the protein identified in the specification as the neuropeptide receptor of SEQ ID NO: 2, the instant invention is incomplete. In the absence of knowledge of the natural substrate or biological significance of this protein, there is no immediately obvious patentable use for it. Since the instant specification does not disclose a "real world" use for the neuropeptide receptor then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

(ii) Applicant argues that a proper inquiry into utility is simply whether one of skill in the art would more likely than not find it specific, substantial and credible that compositions of the invention, which is preferentially expressed in the hypothalamus, would be useful in the prevention and/or treatment of diseases and disorders including obesity. Applicant contends that the asserted utility is specific and substantial. Applicant cites MPEP §2107.01(I) and *In re Cortright*, 49 USPQ2d 1464, 1466 (Fed. Cir. 1999). Applicant concludes that a nexus has been made between the molecule of the instant invention, the hypothalamus, regulation of feeding behavior and disorders such as obesity.

Applicant's arguments have been fully considered but are not found to be persuasive. In the Office Action of 01 November 2004, the previous Examiner made a *prima facie* showing that the claimed invention lacks utility and provided sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing (see pages 3-8). Essentially, Applicant has not provided evidence to demonstrate that the claimed neuropeptide receptor polypeptide is supported by a specific and asserted utility or a well established utility. The Examiner has fully considered all evidence of record and has responded to each substantive element of Applicant's response (see point (i) above). It is noted to Applicant that MPEP § 2107.02 (part VI) also states that "only where the totality of the record continues to show that the asserted utility is not specific, substantial, and credible should a rejection based on lack of utility be maintained".

9. Claims 26-31 and 38-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pg 8-9 of the Office Action of 01 November 2004.

Applicant's arguments (28 February 2005) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the above-mentioned reasons.

Applicant argues that the concerns for 35 USC §112, first paragraph have been addressed in the arguments made for 35 USC §101. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, since Applicant has not provided evidence to demonstrate that the claimed polypeptide has a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

10. However, even if the claimed invention is eventually deemed to have a credible, specific and substantial asserted utility or a well established utility, claims 38-42 would remain rejected under 35 U.S.C. § 112, first paragraph. The basis for

Applicant's arguments (28 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that claim 11 has been amended and no pending claim recites any fragments, domains, mature forms of a secreted protein, variants, alleles, and species homologs of the polypeptide of SEQ ID NO: 2.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, claims 38-42 still recite variants of the amino acid sequence of SEQ ID NO: 2 since the claims are directed to a protein comprising a polypeptide that "is at least 95% identical to amino acid residues 1 to 425 of SEQ ID NO: 2". As discussed in the Office Action of 01

November 2004, certain positions in the polypeptide sequence are critical to the protein's structure/function relationship, e.g., such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. A large quantity of experimentation would be required by the skilled artisan to generate the infinite number of derivatives recited in the claims and screen the same for activity. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. No such variants were made or shown to have activity. Only the polypeptide of SEQ ID NO: 2 is disclosed. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide

activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 112, first paragraph (written description)

11. Claims 38-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth for claims 38-47 at pg 13-15 of the Office Action of 01 November 2004.

Applicant's arguments (28 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. Applicant states that this burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicant possesses the subject matter as of the priority date of the present application. Applicant argues that all of the objectives met by a generic chemical formula are met by the explicit description in the instant specification of a polynucleotide sequence (SEQ ID NO: 1) and the amino acid sequence encoded thereby (SEQ ID NO: 2) and by the instant claims to polypeptides which are at least 95% identical to amino acid residues 1 to 425 of SEQ ID NO: 2. Applicant indicates that the specification contains an adequate written description of the claimed

polypeptides and has provided the skilled artisan with a "generic formula" in the form of the amino acid sequence of SEQ ID NO: 2. Applicant adds that the skilled artisan could easily substitute any given amino acid for any other given amino acid, or add or delete amino acids, such that nothing more than what is described in the specification would be required to identify every single one of the polypeptides comprising amino acid sequences that are 95% identical to the amino acid sequence of SEQ ID NO: 2.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Applicant has not described or shown possession of all polypeptides 95% homologous to SEQ ID NO: 2, that still retain the function of SEQ ID NO: 2. Nor has Applicant described a representative number of species that have 95% homology to SEQ ID NO: 2, such that it is clear that they were in possession of a genus of polypeptides functionally similar to SEQ ID NO: 2. As discussed in the Office Action of 01 November 2004, even one skilled in the art could not envision the detailed chemical structure of all or a significant number of encompassed neuropeptide receptor polypeptides, and therefore, would not know how to make or use them. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. The claimed product itself is required. Applicant made no variant polypeptides, and as recited in the current Written Description Guidelines, Applicants must have invented the subject matter that is claimed and must be in "possession" of the claimed genus (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Furthermore, the broad brush discussion of making and screening for variants in the instant specification does not constitute a disclosure of a representative number of members. No

such variants were made or shown to have activity. Only the polypeptide of SEQ ID NO: 2 is disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factors present in the claims are a partial structure in the form of a recitation of percent identity. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function. Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus.

Claim Rejections - 35 USC § 102

12. Claims 38-41 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Bergsma et al. (U.S. Patent 6,020,157; date of patent 2/1/2000; issued from an application filed 4/30/1997). The basis for this rejection is set forth for claims 11, 26-30, 38-41 at pg 17-18 of the Office Action of 01 November 2004.

Bergsma et al. teach an isolated polypeptide that is 99.8% identical to the amino acid sequence of SEQ ID NO: 2 of the instant application (see also SEQ ID NO: 2 of Bergsma et al.).

Bergsma et al. also disclose fusion proteins comprising said sequence and compositions of said sequence (col 6, 20-21).

Applicant's arguments (28 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that claim 11 has been amended and no longer recites any one of the group "fragment, domain, epitope, mature form, variant, allelic variant, and species homologue", thereby obviating its rejection. Applicant also asserts that the claims of the instant application are entitled to the benefit of priority to PCT International Application PCT/US95/05616, filed May 5, 1995. Applicant states that U.S. 6,020,157 issued from a US application filed on April 30, 1997 and is unavailable as prior art.

Applicant's arguments have been fully considered but are not found to be persuasive. Claims 38-41 still recite an isolated protein comprising a polypeptide which is at least 95% identical to the amino acid residues 1 to 425 of SEQ ID NO: 2. Thus, these claims are anticipated because Bergsma et al. teach an isolated polypeptide that is 99.8% identical to the amino acid sequence of SEQ ID NO: 2 of the instant application.

Furthermore, regarding Applicant's priority benefits, Applicant's claim for priority under 35 U.S.C. 120 is acknowledged. However, the polypeptide of SEQ ID NO: 2 of the instant application is not fully disclosed in many of the prior U.S. nonprovisional and PCT applications Applicant is claiming benefit to. The claimed polypeptide comprising amino acids 1 to 425 of SEQ ID NO: 2 was not fully disclosed until PCT/US00/24518 (9/7/2000). All of the prior U.S. nonprovisional and PCT applications only disclose a neuropeptide receptor 402 amino acids in length. Therefore, the priority date of the claims that recite the polypeptide comprising amino

acid residues 1(2) to 425 of SEQ ID NO: 2 is deemed to be 07 September 2000. This date has been used for the purposes of applying the prior art.

13. Claims 38-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Hagan et al. (U.S. Patent 6,664,229; date of patent 12/16/03; issued from an application filed 12/16/1998). The basis for this rejection is set forth for claims 11, 26-31, 38-42 at pg 18 of the Office Action of 01 November 2004.

Hagan et al. teach an isolated polypeptide that is 99.8% identical to the amino acid sequence of SEQ ID NO: 2 of the instant application (see also SEQ ID NO: 22 of Hagan et al.). Hagan et al. also disclose fusion proteins comprising said sequence, glycosylated forms of said sequence, and compositions of said sequence (col 8, 10, 20).

Applicant's arguments (28 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that claim 11 has been amended and no longer recites any one of the group "fragment, domain, epitope, mature form, variant, allelic variant, and species homologue", thereby obviating its rejection. Applicant also asserts that the claims of the instant application are entitled to the benefit of priority to PCT International Application PCT/US95/05616, filed May 5, 1995. Applicant states that U.S. 6,020,157 issued from a US application filed on April 30, 1997 and is unavailable as prior art.

Applicant's arguments have been fully considered but are not found to be persuasive. Claims 38-42 still recite an isolated protein comprising a polypeptide which is at least 95% identical to the amino acid residues 1 to 425 of SEQ ID NO: 2. Thus, these claims are

anticipated because Hagan et al. teach an isolated polypeptide that is 99.8% identical to the amino acid sequence of SEQ ID NO: 2 of the instant application.

Furthermore, regarding Applicant's priority benefits, Applicant's claim for priority under 35 U.S.C. 120 is acknowledged. However, the polypeptide of SEQ ID NO: 2 of the instant application is not fully disclosed in many of the prior U.S. nonprovisional and PCT applications Applicant is claiming benefit to. The claimed polypeptide comprising amino acids 1 to 425 of SEQ ID NO: 2 was not fully disclosed until PCT/US00/24518 (9/7/2000). All of the prior U.S. nonprovisional and PCT applications only disclose a neuropeptide receptor 402 amino acids in length. Therefore, the priority date of the claims that recite the polypeptide comprising amino acid residues 1(2) to 425 of SEQ ID NO: 2 is deemed to be 07 September 2000. This date has been used for the purposes of applying the prior art.

New Claim Rejections - 35 USC § 102

14. Claims 38 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Sakurai et al (Cell 92: 573-585, 1998).

Sakurai et al. teach an isolated polypeptide that is 99.8% identical to the receptor protein of SEQ ID NO: 2 of the instant application (see Figure 2C, "OX1R" of Sakurai et al.; see also sequence alignment attached to the instant Office Action as Appendix A). Sakurai et al. also disclose the "OX1R" polypeptide is produced by CHO cells and HEK293 cells (pg 573, last paragraph through pg 574; pg 577; pg 582, 2nd full paragraph; Figures 1, 3).

As discussed in the previous art rejections, the polypeptide of SEQ ID NO: 2 of the instant application is not fully disclosed in many of the prior U.S. nonprovisional and PCT

applications Applicant is claiming benefit to. The claimed polypeptide comprising amino acids 1 to 425 of SEQ ID NO: 2 was not fully disclosed until PCT/US00/24518 (9/7/2000). All of the prior U.S. nonprovisional and PCT applications only disclose a neuropeptide receptor 402 amino acids in length. Therefore, the priority date of the claims that recite the polypeptide comprising amino acid residues 1(2) to 425 of SEQ ID NO: 2 is deemed to be 07 September 2000. This date has been used for the purposes of applying the prior art.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
03 January 2005

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER

Appendix A

```
DR   GO; GO:0016499; F:orexin receptor activity; IEA.
DR   GO; GO:0004872; F:receptor activity; IEA.
DR   GO; GO:0001584; F:rhodopsin-like receptor activity; IEA.
DR   GO; GO:0007186; P:G-protein coupled receptor protein signalin. . .; IEA.
DR   InterPro; IPR000276; GPCR_Rhodpsn.
DR   InterPro; IPR000204; Orexin_receptor.
DR   InterPro; IPR004059; Orexin_receptor1.
DR   Pfam; PF00001; 7tm_1; 1.
DR   PRINTS; PR00237; GPCRRHODOPSN.
DR   PRINTS; PR01521; OREXIN1R.
DR   PRINTS; PR01064; OREXINR.
DR   PROSITE; PS00237; G_PROTEIN_RECEP_F1_1; UNKNOWN_1.
DR   PROSITE; PS50262; G_PROTEIN_RECEP_F1_2; 1.
KW   Receptor.
SQ   SEQUENCE   425 AA;  47535 MW;  B650B37F3A2CA096 CRC64;

  Query Match             100.0%;  Score 2218;  DB 2;  Length 425;
  Best Local Similarity   99.8%;  Pred. No. 1.4e-144;
  Matches  424;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MEPSATPGAQMGVPPGSREPSPVPPDYEDEFLRYLWRDYLYPKQYEWVLIAAYVAVFVVA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MEPSATPGAQMGVPPGSREPSPVPPDYEDEFLRYLWRDYLYPKQYEWVLIAAYVAVFVVA 60

Qy         61 LVGNTLVCLAVWRNHHMRTVTNYFIVNLSLADVLVTAICLPASLLVDITESWLFGHALCK 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 LVGNTLVCLAVWRNHHMRTVTNYFIVNLSLADVLVTAICLPASLLVDITESWLFGHALCK 120

Qy        121 VIPYLQAVSVSVAVLTLSFIALDRWYAICHPLLFKSTARRARGSILGIWAVSLAIMVPQA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 VIPYLQAVSVSVAVLTLSFIALDRWYAICHPLLFKSTARRARGSILGIWAVSLAIMVPQA 180

Qy        181 AVMECSSVLPELANRTRLFSVCDERWADDLYPKIYHSCFFIVTYLAPLGLMAMAYFQIFR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AVMECSSVLPELANRTRLFSVCDERWADDLYPKIYHSCFFIVTYLAPLGLMAMAYFQIFR 240

Qy        241 KLWGRQIPGTTSALVRNWKRPSDQLGDLEQGLSGEPQPRARAFLAEVKQMRARRKTAKML 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KLWGRQIPGTTSALVRNWKRPSDQLGDLEQGLSGEPQPRARAFLAEVKQMRARRKTAKML 300

Qy        301 MVVLLVFALCYLPISVLNVLKRVFGMFRQASDREAVYACFTFSHWLVYANSAANPIIYNF 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 MVVLLVFALCYLPISVLNVLKRVFGMFRQASDREAVYACFTFSHWLVYANSAANPIIYNF 360

Qy        361 LSGKFREQFKAAFSCCLPGLGPCGSLKAPSPRSSASHKSLSLQSRCSVSKISEHVVLTSV 420
              ||||||||||||||||||||||||||||||||||||||||||:||||||||||||||||
Db        361 LSGKFREQFKAAFSCCLPGLGPCGSLKAPSPRSSASHKSLSLQSRCSISKISEHVVLTSV 420

Qy        421 TTVLP 425
              |||||
Db        421 TTVLP 425


RESULT 2
OX1R_HUMAN
ID   OX1R_HUMAN      STANDARD;      PRT;   425 AA.
AC   O43613;
```

```
DT   30-MAY-2000 (Rel. 39, Created)
DT   30-MAY-2000 (Rel. 39, Last sequence update)
DT   05-JUL-2004 (Rel. 44, Last annotation update)
DE   Orexin receptor type 1 (Ox1r) (Hypocretin receptor type 1).
GN   Name=HCRTR1;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98150861; PubMed=9491897;
RA   Sakurai T., Amemiya A., Ishii M., Matsuzaki I., Chemelli R.M.,
RA   Tanaka H., Williams S.C., Richardson J.A., Kozlowski G.P., Wilson S.,
RA   Arch J.R.S., Buckingham R.E., Haynes A.C., Carr S.A., Annan R.S.,
RA   McNulty D.E., Liu W.-S., Terrett J.A., Elshourbagy N.A., Bergsma D.J.,
RA   Yanagisawa M.;
RT   "Orexins and orexin receptors: a family of hypothalamic neuropeptides
RT   and G protein-coupled receptors that regulate feeding behavior.";
RL   Cell 92:573-585(1998).
RN   [2]
RP   REVIEW.
RX   MEDLINE=21237974; PubMed=11340621; DOI=10.1002/bies.1058;
RA   Hungs M., Mignot E.;
RT   "Hypocretin/orexin, sleep and narcolepsy.";
RL   Bioessays 23:397-408(2001).
RN   [3]
RP   REVIEW.
RX   MEDLINE=21178476; PubMed=11283317;
RA   Willie J.T., Chemelli R.M., Sinton C.M., Yanagisawa M.;
RT   "To eat or to sleep? Orexin in the regulation of feeding and
RT   wakefulness.";
RL   Annu. Rev. Neurosci. 24:429-458(2001).
CC   -!- FUNCTION: Moderately selective excitatory receptor for orexin-A
CC       and, with a lower affinity, for orexin-B neuropeptide. Seems to be
CC       exclusively coupled to the G(q) subclass of heteromeric G
CC       proteins, which activates the phospholipase C mediated signaling
CC       cascade (By similarity).
CC   -!- SUBCELLULAR LOCATION: Integral membrane protein.
CC   -!- SIMILARITY: Belongs to family 1 of G-protein coupled receptors.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; AF041243; AAC39601.1; -.
DR   Genew; HGNC:4848; HCRTR1.
DR   MIM; 602392; -.
DR   GO; GO:0005887; C:integral to plasma membrane; TAS.
DR   GO; GO:0004930; F:G-protein coupled receptor activity; TAS.
DR   GO; GO:0007631; P:feeding behavior; TAS.
DR   GO; GO:0007218; P:neuropeptide signaling pathway; TAS.
DR   GO; GO:0007268; P:synaptic transmission; TAS.
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DR   InterPro; IPR000276; GPCR_Rhodpsn.
DR   InterPro; IPR000204; Orexin_receptor.
DR   InterPro; IPR004059; Orexin_receptor1.
DR   Pfam; PF00001; 7tm_1; 1.
DR   PRINTS; PR00237; GPCRRHODOPSN.
DR   PRINTS; PR01521; OREXIN1R.
DR   PROSITE; PS00237; G_PROTEIN_RECEP_F1_1; 1.
DR   PROSITE; PS50262; G_PROTEIN_RECEP_F1_2; 1.
KW   G-protein coupled receptor; Transmembrane.
FT   DOMAIN        1     46       Extracellular (Potential).
FT   TRANSMEM     47     67       1 (Potential).
FT   DOMAIN       68     80       Cytoplasmic (Potential).
FT   TRANSMEM     81    102       2 (Potential).
FT   DOMAIN      103    119       Extracellular (Potential).
FT   TRANSMEM    120    142       3 (Potential).
FT   DOMAIN      143    164       Cytoplasmic (Potential).
FT   TRANSMEM    165    185       4 (Potential).
FT   DOMAIN      186    216       Extracellular (Potential).
FT   TRANSMEM    217    239       5 (Potential).
FT   DOMAIN      240    298       Cytoplasmic (Potential).
FT   TRANSMEM    299    321       6 (Potential).
FT   DOMAIN      322    336       Extracellular (Potential).
FT   TRANSMEM    337    360       7 (Potential).
FT   DOMAIN      361    425       Cytoplasmic (Potential).
FT   CARBOHYD    194    194       N-linked (GlcNAc. . .) (Potential).
SQ   SEQUENCE   425 AA;  47521 MW;  1634083DE10CA092 CRC64;

  Query Match             99.8%;  Score 2214;  DB 1;  Length 425;
  Best Local Similarity   99.5%;  Pred. No. 2.6e-144;
  Matches  423;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MEPSATPGAQMGVPPGSREPSPVPPDYEDEFLRYLWRDYLYPKQYEWVLIAAYVAVFVVA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MEPSATPGAQMGVPPGSREPSPVPPDYEDEFLRYLWRDYLYPKQYEWVLIAAYVAVFVVA 60

Qy         61 LVGNTLVCLAVWRNHHMRTVTNYFIVNLSLADVLVTAICLPASLLVDITESWLFGHALCK 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 LVGNTLVCLAVWRNHHMRTVTNYFIVNLSLADVLVTAICLPASLLVDITESWLFGHALCK 120

Qy        121 VIPYLQAVSVSVAVLTLSFIALDRWYAICHPLLFKSTARRARGSILGIWAVSLAIMVPQA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 VIPYLQAVSVSVAVLTLSFIALDRWYAICHPLLFKSTARRARGSILGIWAVSLAIMVPQA 180

Qy        181 AVMECSSVLPELANRTRLFSVCDERWADDLYPKIYHSCFFIVTYLAPLGLMAMAYFQIFR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AVMECSSVLPELANRTRLFSVCDERWADDLYPKIYHSCFFIVTYLAPLGLMAMAYFQIFR 240

Qy        241 KLWGRQIPGTTSALVRNWKRPSDQLGDLEQGLSGEPQPRARAFLAEVKQMRARRKTAKML 300
              |||||||||||||||||||||||||||||||||||| ||||||||||||||||||||||
Db        241 KLWGRQIPGTTSALVRNWKRPSDQLGDLEQGLSGEPQPRGRAFLAEVKQMRARRKTAKML 300

Qy        301 MVVLLVFALCYLPISVLNVLKRVFGMFRQASDREAVYACFTFSHWLVYANSAANPIIYNF 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 MVVLLVFALCYLPISVLNVLKRVFGMFRQASDREAVYACFTFSHWLVYANSAANPIIYNF 360

Qy        361 LSGKFREQFKAAFSCCLPGLGPCGSLKAPSPRSSASHKSLSLQSRCSVSKISEHVVLTSV 420
              ||||||||||||||||||||||||||||||||||||||||||||||:||||||||||||
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Db        361 LSGKFREQFKAAFSCCLPGLGPCGSLKAPSPRSSASHKSLSLQSRCSISKISEHVVLTSV 420

Qy        421 TTVLP 425
              |||||
Db        421 TTVLP 425


RESULT 3
OX1R_RAT
ID   OX1R_RAT       STANDARD;      PRT;   416 AA.
AC   P56718;
DT   30-MAY-2000 (Rel. 39, Created)
DT   30-MAY-2000 (Rel. 39, Last sequence update)
DT   05-JUL-2004 (Rel. 44, Last annotation update)
DE   Orexin receptor type 1 (Ox1r) (Hypocretin receptor type 1).
GN   Name=Hcrtr1;
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX   NCBI_TaxID=10116;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=98150861; PubMed=9491897;
RA   Sakurai T., Amemiya A., Ishii M., Matsuzaki I., Chemelli R.M.,
RA   Tanaka H., Williams S.C., Richardson J.A., Kozlowski G.P., Wilson S.,
RA   Arch J.R.S., Buckingham R.E., Haynes A.C., Carr S.A., Annan R.S.,
RA   McNulty D.E., Liu W.-S., Terrett J.A., Elshourbagy N.A., Bergsma D.J.,
RA   Yanagisawa M.;
RT   "Orexins and orexin receptors: a family of hypothalamic neuropeptides
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RP   REVIEW.
RX   MEDLINE=21237974; PubMed=11340621; DOI=10.1002/bies.1058;
RA   Hungs M., Mignot E.;
RT   "Hypocretin/orexin, sleep and narcolepsy.";
RL   Bioessays 23:397-408(2001).
RN   [3]
RP   REVIEW.
RX   MEDLINE=21178476; PubMed=11283317;
RA   Willie J.T., Chemelli R.M., Sinton C.M., Yanagisawa M.;
RT   "To eat or to sleep? Orexin in the regulation of feeding and
RT   wakefulness.";
RL   Annu. Rev. Neurosci. 24:429-458(2001).
CC   -!- FUNCTION: Moderately selective excitatory receptor for orexin-A
CC       and, with a lower affinity, for orexin-B neuropeptide. Seems to be
CC       exclusively coupled to the G(q) subclass of heteromeric G
CC       proteins, which activates the phospholipase C mediated signaling
CC       cascade.
CC   -!- SUBCELLULAR LOCATION: Integral membrane protein.
CC   -!- TISSUE SPECIFICITY: Highly expressed in the brain in the
CC       prefrontal cortex, hippocampus, paraventricular thalamus,
CC       ventromedial hypothalamus, arcuate nucleus, dorsal raphe nucleus,
CC       and locus coeruleus. Not detected in the spleen, lung, liver,
CC       skeletal muscle, kidney and testis. Orexin receptor mRNA
CC       expression has also been reported in the adrenal gland, enteric
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